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DIAGNOSTIC CRITERIA FOR PNEUMONIA OF ATYPICAL ETIOLOGY IN CHILDREN.

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Abstract: Despite numerous scientific studies, the problem of pneumonia in children, especially with atypical etiology, continues to be unresolved, which is associated with the difficulty of early diagnosis of the etiological factor, the peculiarities of the clinical and laboratory manifestations of the disease. o'2,5,9g'. From the timely detection of the etiological factor of atypical pneumonia, the effectiveness of antibiotic therapy is largely determined, which dramatically affects the course and outcome of the disease, and cultural diagnosis is difficult, since Myc. pneumoniae and Chl. pneumoniae, being intracellular pathogens, are not detected by sputum smear microscopy, with standard bacteriological culture of sputum or blood.

Keywords: diagnostics, atypical pneumonia, children

Relevance. According to the World Health Organization, pneumonia is the most important infectious cause of childhood death worldwide, accounting for 15% of all deaths in children under 5 years of age. The WHO and UNICEF Global Action Plan aims to accelerate the fight against pneumonia by improving prevention and treatment. The search for diagnostic methods for etiological verification and improvement of methods of pathogenetic therapy of pneumonia in children continues. [3,6,10]

At present, the stability of Mus. pneumoniae to macrolides for 2017–2018. was about 15% (11), while it is proved that josamycin has a high microbiological activity, minimal side effects than azithromycin and clarithromycin [1,4,7,12]. In this regard, the drug of choice for ABT in atypical pneumonia was josamycin, which was prescribed in the form of Vilprafen ® at the rate of 30-50 mg/kg/day, in 2-3 oral doses. Course 7–10 days. Numerous studies on the efficacy of resistol (Pelargonium sidoides EPs®7630) in respiratory diseases indicate clinical efficacy and safety in children. The drug in diseases reduces the number of etiological pathogens, exhibits immunomodulatory properties, affects the activity of immune defense, normalizing the levels of IL-15 and IL-6 in the blood serum, which increases the nonspecific resistance of the body [8,11,13,14]. In this regard, we used Resistol, which was prescribed to children from 1 to 6 years old: 10 drops 3 times a day, from 6 to 12 years old, 20 drops 3 times a day. The course of treatment is 7-10 days.

The effectiveness of therapy in patients was assessed by the regression of pathological clinical symptoms of the disease, by the dynamics of normalization of laboratory and instrumental data, as well as by changes in the indicators of special research methods.

Purpose of the research to study the diagnostic criteria for pneumonia with atypical etiology in children.

Materials and methods of the research. At stage 2, to determine the effectiveness of the modified therapy, patients of group I with mycoplasmal etiology were divided into: group Ia - 30 patients who received traditional therapy and group Ib - 30 patients who received josamycin and resistol in combination with traditional therapy; patients of group II with chlamydial etiology were divided into: group IIa - 30 patients who received traditional therapy and group IIb - 30 patients who received josamycin and resistol in the complex of traditional therapy. Josamycin was administered at 30-50 mg/kg in 2-3 doses per day orally, Resistol for children from 1 to 6 years old 10 drops 3 times a day, from 6 to 12 years old 20 drops 3 times a day. The drugs were used throughout the course of treatment. Patients of group III - 30 patients received traditional therapy.

In patients in groups Ib (mycoplasmal pneumonia) and IIb (chlamydial pneumonia) with modified therapy, josamycin and resistol were included in the complex of traditional therapy.

Results of the research. The results of a comparative analysis of the studied parameters (table 1) in patients with etiologically verified pneumonia Myc Pneumoniae (group I) and typical pneumonia (group III) showed that the distribution of children by age that contributed to the incidence structure made it possible to establish that the largest number of children with M. Pneumoniae belonged to the age group over 6 years (56.7%), compared with patients with typical etiology (13.3%) with significant significance (OR=8.50; P<0.001, CI=2.64 - 27.39; $\chi 2$= 15.39; p=0.001). Among other age groups, there was no significant difference in the structure of the frequency of diseases depending on the etiological factor.

Table 1

The frequency of anamnestic data and clinical manifestations in community-acquired pneumonia in patients

indicator	Detection frequency (%)		OR	χ2	P	ДИ min	ДИ max
	I group	III group					
Age							
Up to 1 year	6,7	40,0	0,11	15,20	0,000	0,03	0,37
1 year	36,7	46,7	0,66	0,83	0,361	0,27	1,61
6 year	56,7	13,3	8,50	15,39	0,001	2,64	27,39
boys	43,3	63,3	0,44	3,20	0,074	0,18	1,09
Girls	56,7	36,7	2,26	3,20	0,074	0,92	5,56
The onset of the disease							
Acute	31,7	83,3	0,09	21,37	0,001	0,03	0,28
gradual	68,3	16,7	10,79	21,37	0,001	3,58	32,53

Medium	81,7	56,7	3,41	6,39	0,011	1,29	9,02
heavy	18,3	36,7	0,39	3,64	0,056	0,14	1,04
Extremely heavy	0,0	6,7	0,00	4,09	0,043	-	-
Temperature							
<37,0^0 C	15,0	3,3	5,12	2,76	0,097	0,62	42,45
37,1-37,9^{0}C	55,0	13,3	7,94	14,34	0,001	2,47	25,57
38,0-39,0^{0}C	26,7	53,3	0,32	6,21	0,013	0,13	0,80
> 39,0^{0}C	3,3	30,0	0,08	13,26	0,001	0,02	0,40
Cough							
Dry cough	46,7	23,3	2,88	4,58	0,032	1,07	7,71
Wet	53,3	76,7	0,35	4,58	0,032	0,13	0,93
Sputum							

Sputum							
meager	71,7	13,3	16,44	27,28	0,001	4,99	54,2
Abundant	28,3	86,7	0,06	27,28	0,001	0,02	0,20
Percussion in the lungs							
Clear lung sound	13,3	10,0	1,38	0,21	0,649	0,34	5,65
Shortening, blunting	86,7	90,0	0,72	0,21	0,649	0,18	2,95
Auscultatory in the lungs							
hard breathing	93,3	36,7	24,18	33,76	0,001	6,88	85,01
Weakened breathing	6,7	63,3	0,04	33,76	0,001	0,01	0,15
Wheezing in the lungs							
Crepitant	6,7	23,3	0,23	5,18	0,023	0,06	0,88
Wet	68,3	53,3	1,89	1,94	0,164	0,77	4,65

Respiratory failure							
RF 0.	21,7	3,3	8,02	5,12	0,024	1,00	64,59
RF 1.	50,0	26,7	2,75	4,46	0,035	1,06	7,14
RF 2.	28,3	60,0	0,26	8,44	0,004	0,10	0,66
RF 3.	0,0	10,0	0,00	6,21	0,013	-	-
Concomitant diseases, complications							
Rhinitis	6,7	10,0	0,64	0,31	0,578	0,13	3,08
Conjunctivitis	11,7	10,0	1,19	0,06	0,813	0,28	4,97
Pharyngitis	30,0	10,0	3,86	4,47	0,034	1,04	14,36
Otitis	6,7	3,3	2,07	0,42	0,515	0,22	19,39
Increase l / y	10,0	6,7	1,56	0,27	0,600	0,29	8,22

Intoxication	8,3	70,0	0,04	37,02	0,001	0,01	0,13
biofeedback	21,7	3,3	8,02	5,12	0,024	1,00	64,59
Familial nature of pneumonia	21,7	3,3	8,02	5,12	0,024	1,00	64,59

In mycoplasmal pneumonia, the onset of the disease was mainly associated with a gradual increase in clinical symptoms (68.3%), which was a significantly significant criterion in comparison with pneumonia of typical etiology (p=0.001).

Upon admission to the hospital, the state of moderate severity in children was significantly more often observed with mycoplasmal pneumonia (81.7%), in contrast to the disease caused by typical flora (56.7%), with their significant difference (p=0.011).

With mycoplasmal pneumonia, the disease in 70.0% of cases occurs against the background of normal or subfebrile temperature, febrile temperature in 26.7% and in isolated cases in patients (3.3%) was recorded above 39.00 C, which significantly differed from the frequency characteristics with pneumonia of typical etiology - 16.6%, 53.3% and 30.0%, respectively. At the same time, fever in the range of 37.1-37.90C in pneumonia with M. Pneumoniae had significant differences from the typical flora (p=0.001).

The main complaint addressed by patients with mycoplasmal pneumonia was a cough that appeared from the first days of the disease having a dry, pertussis-like character (47.6%), later manifested by scanty sputum difficult to separate (71.7%), which was less common in typical pneumonia - 23.3% and 13.3%, respectively (p-0.001).

Physical data in children with mycoplasmal pneumonia were very scarce. Quite rarely, pulmonary sound was determined percussion - 13.3% of cases, auscultatory in most cases, hard breathing - 93.3%, which, in comparison with pneumonia of typical etiology, had a significant difference. The characteristics of wheezing in the lungs did not have a significant difference in contrast to pneumonia of typical etiology.

In mycoplasma pneumonia, high rates of absence (21.7%) or slight dyspnea (50.0%) were observed, which was a significant difference compared to typical pneumonia.

When analyzing the frequency of concomitant diseases and complications in children with mycoplasma pneumonia in comparison with pneumonia of typical etiology, the tendency to develop pharyngitis was 30.0%, broncho-obstructive syndrome was 21.7%, and a high frequency of the "family" nature of the disease was determined - 21.7% of cases respectively.

The data of the analysis, clearly demonstrated in Figure 2, allow us to recommend as additional criteria for the etiological diagnosis of pneumonia caused by Myc. Pneumoniae: age of children older than 6 years, gradual development, "familial" nature of the

disease, moderate condition, subfebrile temperature, unproductive, obsessive, dry cough with scanty sputum difficult to separate, absence or RF 1 degree, presence of pharyngitis and broncho-obstructive syndrome.

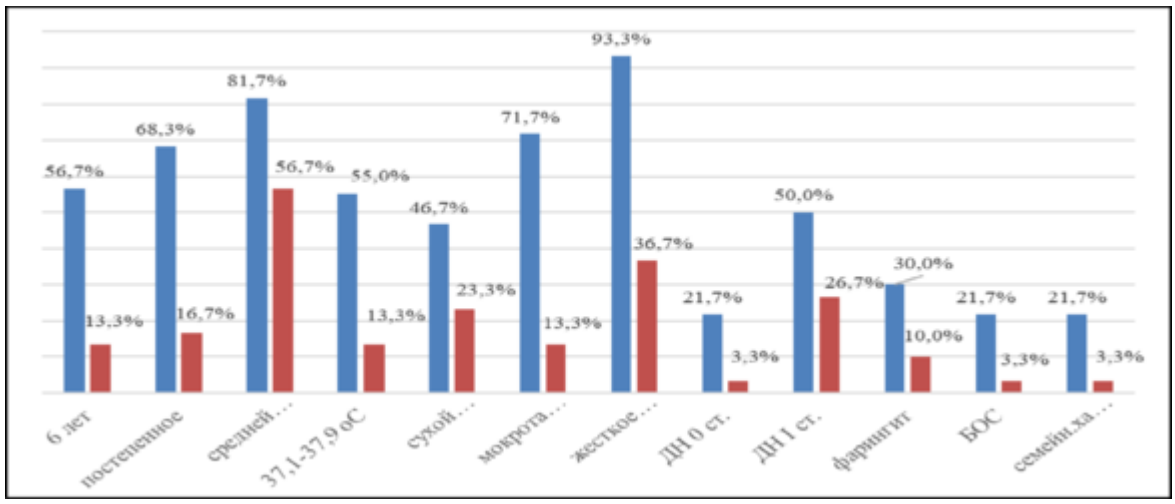

Figure 1 Diagnostic value of anamnestic data and clinical manifestations in community-acquired pneumonia in patients.

Not – I группа, – III группа.

In the study of CRP and PCT, conducted upon admission to the hospital in patients with mycoplasma (group I) and chlamydial (group II) pneumonia, a significant difference was found in almost all the studied indicators in relation to the control standards (table 2).

table 2

Indicators of inflammation markers and cytokines in patients with atypical pneumonia (M±m).

Parameters	Norm	Group I	Group II	P_1	P_2	P_3
СРБ (мг/л)	3,3±0,2	32,3±0,9	30,8±1,0	<0,001	<0,001	>0,2
ПКТ (нг/л)	0,16±0,01	1,08±0,02	1,04±0,02	<0,001	<0,001	>0,2
IL-4 пг/мл	4,8±0,3	15,8±0,5	18,0±0,6	<0,001	<0,001	<0,01
IL-6 пг/мл	16,3±0,7	46,1±1,4	48,8±1,5	<0,001	<0,001	>0,2
TNF-α пг/мл	24,5±0,8	61,4±1,9	65,9±2,0	<0,001	<0,001	>0,2

Note: P1 - significance of differences between standard values and mycoplasma pneumonia, P2 - between standard values and chlamydial pneumonia, P3 - between mycoplasma and chlamydial pneumonia.

Thus, the content of CRP by 9.8 times and PCT by 6.7 times in mycoplasma, CRP by 8.9 times and PCT by 6.3 times in chlamydial pneumonia exceeded the standard values ($P<0.001$). At the same time, there was a slight excess of these indicators in pneumonia of mycoplasmal etiology in relation to chlamydial pneumonia ($P>0.1$, $P>0.2$).

The revealed regularities in the assessment of the concentration of inflammatory biomarkers CRP and PCT in the blood of patients indicate a pronounced activity of the inflammatory process in pneumonia caused by the pathological influence of Myc. pneumoniae and Chl. pneumoniae on a patient and, in combination with other clinical

and laboratory parameters, will allow monitoring the disease and evaluating the effectiveness of drug therapy.

The introduction of CRP and PCT into the list of clinical algorithms for the management of SARS in children will provide an opportunity to obtain additional criteria for diagnosing and treating patients, which in turn will allow making informed decisions in pediatric practice.

Analysis of the obtained data (Table 2) showed that in patients with atypical pneumonia there are significant increases in endogenous production of both anti-inflammatory - IL-4, and pro-inflammatory cytokines - IL-6 and TNF-?, more than 3.2, 2.9 and 2.5 times for mycoplasma and 3.6, 3.1 and 2.7 times for chlamydial etiology, respectively, compared with the standard values ($P<0.001$).

The concentrations of the levels of pro-inflammatory cytokines (IL-6 and TNF-?), with their significant predominance relative to the norm, did not have significant deviations relative to Myc. pneumoniae and Chl. pneumoniae pneumonia ($P>0.2$).

At the same time, the relatively maximum increase in the concentration of IL-4 in chlamydial pneumonia (18.0±0.6 pg/ml) in comparison with mycoplasmal pneumonia (15.8±0.5 pg/ml) was significant in comparison with each other ($P<0.01$). More pronounced hypercytokinemia of IL-4 in group I patients characterizes an increased immune response in mycoplasmal pneumonia, which is associated with the inhibitory properties of this cytokine, which enhances the protective effect in comparison with chlamydial pneumonia

The analysis data showed that in the formation of the pneumonic process in children by atypical etiological factors (Mus. pneumoniae and Chl. pneumoniae), a significant role is played by hyperproduction of anti-inflammatory cytokines and a decrease in the level of pro-inflammatory cytokines.

Conclusion. The results of the studies showed that immunological disorders in sick children with atypical pneumonia are characterized by a significant increase in pro-inflammatory and anti-inflammatory cytokines in comparison with the standard values ($P<0.001$). In patients with mycoplasmal pneumonia, the significance of IL-4 is more pronounced in comparison with chlamydial pneumonia.

The revealed violations of cytokine indicators indicate the possibility of their use as promising markers in the early diagnosis of the etiological factor and will increase the possibility of corrective therapy for pneumonia of atypical etiology.

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